IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s):	Turner, Jr. *et al.*	Group Art Unit:	1647
Application No.:	09/689,911	Examiner:	B. Bunner
Filed:	10/11/2000	Atty. Docket No.:	LEX-0068-USA

Title: Polynucleotides Encoding Human Galanin Family Proteins (As Amended)

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AMENDMENT AND RESPONSE TO OFFICE ACTION DATED SEPTEMBER 24, 2002

Assistant Commissioner for Patents
Arlington, VA 22202

Sir:

The Applicants acknowledge the receipt of the Office Action ("the Action") mailed on September 24, 2002 (Paper No. 13), which has been carefully reviewed and studied. The Examiner is respectfully requested to enter the following amendments. Reexamination and reconsideration of the application is requested in view of the following amendments and remarks. In order to facilitate the Examiner's evaluation of the application, Applicants have attempted to address the objections and rejections in Paper No. 13 in the same order in which they were originally raised.

A Petition for an Extension of Time of two months to and including February 24, 2003, and authorization to deduct the fee as required under 37 C.F.R. § 1.17(a)(2) from Applicants' representatives Deposit Account are included. The response is thus timely filed. Applicants believe no fees in addition to the fee for the extension of time are due in connection with this response. However, the Commissioner is authorized to charge any additionally required fees or credit any overpayment to Deposit Account No. 50-0892.

AMENDMENT

In the claims:

Please amend claim 2 so that the text of the amended claim reads as follows:

2. (Twice Amended) An isolated nucleic acid molecule comprising a nucleotide sequence that:

(a) encodes the amino acid sequence shown in SEQ ID NO: 2; and

(b) hybridizes to the nucleotide sequence of SEQ ID NO: 1 or the complement thereof under highly stringent conditions of 0.5 M $NaHPO_4$, 7% sodium dodecyl sulfate (SDS) and 1 mM EDTA at 65°C and washing in 0.1x SSC/0.1%SDS at 68°C.

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RESPONSE

I. Status of the Claims

No claims have been cancelled. Claim 2 has been amended. No new claims have been added. Claims 1-8 are therefore presently pending in the case. For the convenience of the Examiner, a clean copy of the pending claims is attached hereto as **Exhibit A**. In compliance with 37 C.F.R. § 1.121(c)(1)(ii), a marked up copy of the original claims is attached hereto as **Exhibit B**.

II. Support for the Amended Claim

Claim 2 has been amended to recite specific highly stringent hybridization conditions. Support for this claim can be found throughout the specification as originally filed, with particular support being found at least from page 3, line 32 through page 4, line 5.

It will be understood that no new matter is included within the amended claim.

III. Oath/Declaration

The Action notes that the declaration is defective because it does not identify the mailing or post office address of each inventor. Applicants submit herewith a supplemental declaration in compliance

with 37 C.F.R. § 1.67(a), which identifies the application by application number and filing date.

IV. Rejection of Claims 1-8 Under 35 U.S.C. § 101

The Action first rejects claims 1-8 under 35 U.S.C. § 101, as allegedly lacking a patentable utility. Applicants respectfully traverse.

The Action seems to base this rejection on the assertion that "(t)he specification of the instant application does not disclose the function of the polynucleotide and polypeptide" (Action at page 4). However, Applicants note for the record that the instant application, at least at page 1, lines 32-36, identifies the presently claimed galanin family sequences as involved in a number of functions, including a role in "inflammation" (specification at page 1, line 34). This phenotype has in fact been confirmed in genetically engineered mice that lack the murine homolog of the presently claimed sequence (support for such "knockout" mice can be found, for example, in the specification at page 1, lines 14-15, and page 2, lines 27-28). Mice were created in which a portion of the murine homolog of the presently claimed galanin family sequence was deleted, and then subjected to a peritoneal inflammation assay to assess the immune system by challenge with zymosan, an extract of yeast cells. The homozygous animals showed an increase in total white blood cells compared to a wild-type control, consistent with, as set forth in the instant application, the stated role of this protein in inflammation. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Furthermore, given the medical relevance of the presently claimed sequences, those of skill in the art would readily appreciate the importance of tracking the expression of the genes encoding the described proteins, as described in the specification as originally filed, at least at page 5, lines 2-4. In particular, the specification describes how the described sequences can be represented using a gene chip format to provide a high throughput analysis of the level of gene expression. Such "DNA chips" clearly have utility, as evidenced by hundreds of issued U.S. Patents, as exemplified by U.S. Patent Nos. 5,445,934, 5,556,752, 5,744,305, 5,837,832, 6,156,501 and 6,261,776. Evidence of the "real world" substantial utility of the present invention is further provided by the fact that there is an entire industry established based on the use of gene sequences or fragments thereof in a gene chip format. Perhaps the most notable gene chip company is Affymetrix. However, there are many companies which have, at one time or another, concentrated on the use of gene sequences or fragments, in gene

chip and non-gene chip formats, for example: Gene Logic, ABI-Perkin-Elmer, HySeq and Incyte. In addition, two such companies (Agilent acquired by American Home Products and Rosetta acquired by Merck) were viewed to have such "real world" value that they were acquired by large pharmaceutical companies for significant sums of money. The "real world" substantial industrial utility of gene sequences or fragments would, therefore, appear to be widespread and well established. Clearly, there can be no doubt that the skilled artisan would know how to use the presently claimed sequences (see Section V, below), strongly arguing that the claimed sequences have utility. Given the widespread utility of such "gene chip" methods using *public domain* gene sequence information, there can be little doubt that the use of the presently described *novel and medically relevant* sequences would have great utility in such DNA chip applications. As the present sequences are specific markers of the human genome (see below), and such specific markers are targets for the discovery of drugs that are associated with human disease, as described above, those of skill in the art would instantly recognize that the present nucleotide sequences would be ideal, novel candidates for assessing gene expression using such DNA chips. Clearly, compositions that enhance the utility of such DNA chips, such as the presently claimed nucleotide sequences, must in themselves be useful. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Although Applicants need only make one credible assertion of utility to meet the requirements of 35 U.S.C. § 101 (*Raytheon v. Roper*, 220 USPQ 592 (Fed. Cir. 1983); *In re Gottlieb*, 140 USPQ 665 (CCPA 1964); *In re Malachowski*, 189 USPQ 432 (CCPA 1976); *Hoffman v. Klaus*, 9 USPQ2d 1657 (Bd. Pat. App. & Inter. 1988)), as a further example of the utility of the presently claimed polynucleotides, as described in the specification at least at page 7, line 20, the present nucleotide sequence has a specific utility in determining the genomic structure of the corresponding human chromosome, for example mapping the protein encoding regions. This is evidenced by the fact that SEQ ID NO:1 can be used to map the 5 coding exons on human chromosome 19 (present within Genbank Accession Number AC024580, which is a clone from human chromosome 19; alignment and first page from Genbank record shown in **Exhibit C**). Clearly, the present polynucleotide provides exquisite specificity in localizing the specific region of human chromosome 19 that contains the gene encoding the given polynucleotide, a utility not shared by virtually any other nucleic acid sequences. In fact, it is this specificity that makes this particular sequence so useful. Early gene mapping techniques

relied on methods such as Giemsa staining to identify regions of chromosomes. However, such techniques produced genetic maps with a resolution of only 5 to 10 megabases, far too low to be of much help in identifying specific genes involved in disease. The skilled artisan readily appreciates the significant benefit afforded by markers that map a specific locus of the human genome, such as the present nucleic acid sequence. Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Equally significant is that the claimed polynucleotide sequences define how the encoded exons are actually spliced together to produce an active transcript (*i.e.*, the described sequences are useful for functionally defining exon splice-junctions). The presently claimed sequence clearly identified the intron/exon boundaries, as described above. The specification details that "sequences derived from regions adjacent to the intron/exon boundaries of the human gene can be used to design primers for use in amplification assays to detect mutations within the exons, introns, splice sites (*e.g.*, splice acceptor and/or donor sites), *etc.*, that can be used in diagnostics and pharmacogenomics" (specification at page 7, lines 21-26). Thus, the present claims clearly meet the requirements of 35 U.S.C. § 101.

Finally, while Applicants are well aware of the new Utility Guidelines set forth by the USPTO, it has been long established that the current rules regarding the examination of patent applications is and always has been the patent laws as set forth in 35 U.S.C. and the patent rules as set forth in 37 C.F.R., not the Manual of Patent Examination Procedure or particular guidelines for patent examination set forth by the USPTO. Furthermore, it is the job of the judiciary, not the USPTO, to interpret these laws and rules. Applicants point out that guidelines that are not consistent with the patent laws, or the interpretation of these laws by the judicial branch, are not the final word in determining whether or not claims comply with any particular section of the patent laws. Applicants are unaware of any significant recent changes in either 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit that is in keeping with the new Utility Guidelines set forth by the USPTO. This is underscored by numerous patents that have been issued over the years that claim nucleic acid fragments that do not comply with the new Utility Guidelines. As examples of such issued U.S. Patents, the Examiner is invited to review U.S. Patent Nos. 5,817,479, 5,654,173, and 5,552,281 (each of which claim short polynucleotides), none of which contain examples of the "real-world" utilities that seem to be required in the Action. As issued U.S. Patents are presumed to meet all of the requirements

for patentability, including 35 U.S.C. §§ 101 and 112, first paragraph (see Section V below), Applicants submit that the presently claimed polynucleotides must also meet the requirements of 35 U.S.C. § 101. While Applicants understand that each patent application is examined on the basis of its individual merits, Applicants are unaware of any changes to 35 U.S.C. § 101, or in the interpretation of 35 U.S.C. § 101 by the Supreme Court or the Federal Circuit, since the issuance of these patents that render the subject matter claimed in these patents, which is similar to the subject matter in question in the present application, as suddenly non-statutory or failing to meet the requirements of 35 U.S.C. § 101. The requirement of Applicants to meet a different standard of utility in the present case would be arbitrary and capricious, and cannot stand.

For each of the foregoing reasons, as well as the reasons set forth in Applicants' response filed on July 1, 2002 to the previous Office Action mailed on April 1, 2002, Applicants submit that as the presently claimed nucleic acid molecules have been shown to have a substantial, specific, credible and well-established utility, the rejection of claims 1-8 under 35 U.S.C. § 101 has been overcome, and request that the rejection be withdrawn.

V. Rejection of Claims 1-8 Under 35 U.S.C. § 112, First Paragraph

The Action next rejects claims 1-8 under 35 U.S.C. § 112, first paragraph, since allegedly one skilled in the art would not know how to use the invention, as the invention allegedly is not supported by a specific, substantial, and credible utility or a well-established utility. Applicants respectfully traverse.

Applicants submit that as claims 1-8 have been shown to have "a specific, substantial, and credible utility", as detailed in section IV above, the present rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, cannot stand.

Applicants therefore request that the rejection of claims 1-8 under 35 U.S.C. § 112, first paragraph, be withdrawn.

VI. Rejection of Claim 2 Under 35 U.S.C. § 112, Second Paragraph

The Action next rejects claim 2 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the invention.

The Action rejects claim 2 as allegedly indefinite based on the term "highly stringent hybridization conditions", because the specific hybridization and washing conditions are not recited in the claim. Applicants stress that "a claim need not 'describe' the invention, such description being the role of the disclosure". *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 1 USPQ2d 1081, 1088 (Fed. Cir. 1986). However, while Applicants submit that the term is sufficiently definite, as a number of highly stringent hybridization conditions are defined in the specification and would be known to those of skill in the art, solely in order to progress the case more rapidly toward allowance the claim has been revised to recite specific highly stringent hybridization conditions. As the specification provides specific teaching regarding these highly stringent hybridization conditions, at least from page 3, line 32 through page 4, line 5, Applicants submit that revised claim 2 even more clearly meets the requirements of 35 U.S.C. § 112, second paragraph. Applicants therefore request withdrawal of this rejection.

VII. Conclusion

The present document is a full and complete response to the Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance, and such favorable action is respectfully requested. Should Examiner Bunner have any questions or comments, or believe that certain amendments of the claims might serve to improve their clarity, a telephone call to the undersigned Applicants' representative is earnestly solicited.

Respectfully submitted,

February 21, 2003
Date

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